



# NORTHWEST AIDS EDUCATION AND TRAINING CENTER

## Pre-exposure prophylaxis (PrEP) for HIV prevention

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Presentation prepared by:  
Presenter  
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# Disclosure

- No medication is currently licensed for pre-exposure prophylaxis (PrEP) against HIV infection.
- The speaker has received research funding related to PrEP from the Bill & Melinda Gates Foundation and the US National Institutes of Health, with study medication donated by Gilead Sciences. He has no other financial conflicts of interest.

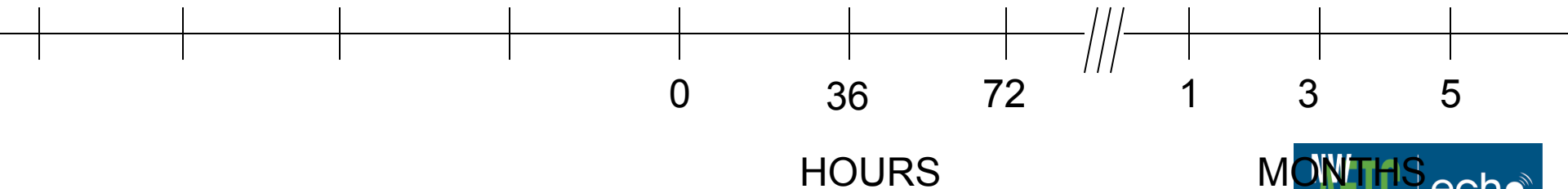
# Learning objectives

- To understand the concept of pre-exposure prophylaxis (PrEP) for HIV prevention.
- To see the data from the two pivotal studies in men who have sex with men and heterosexual men and women.
- To understand the importance of regular HIV testing and periodic renal safety monitoring in persons taking PrEP.

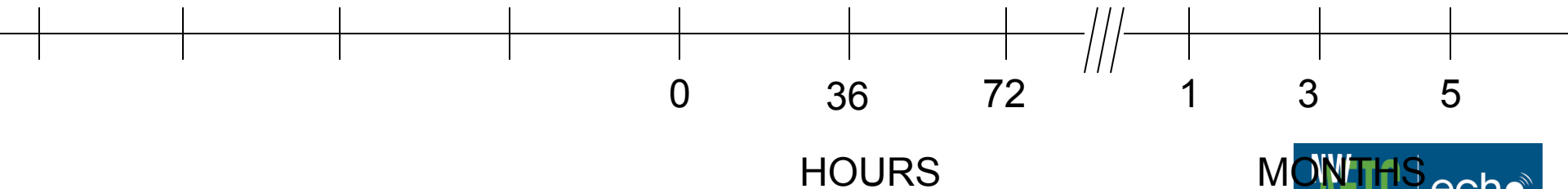
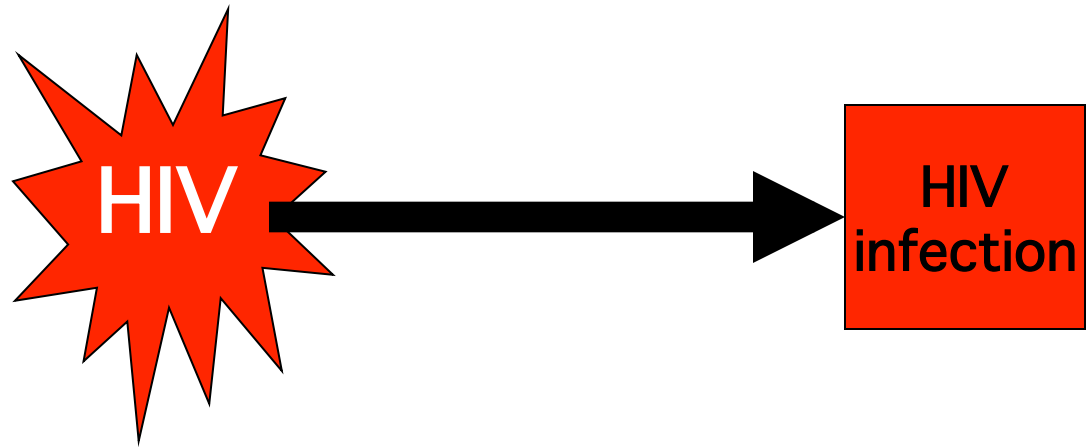
# Pre-exposure prophylaxis (PrEP): the hypothesis

- In PrEP, an HIV uninfected individual uses an antiretroviral medication(s) ahead of an HIV exposure.
- By having the antiretroviral in blood/tissues, PrEP may make it so that HIV is unable to establish infection.
- Analogy to prophylaxis for malaria or Pneumocystis

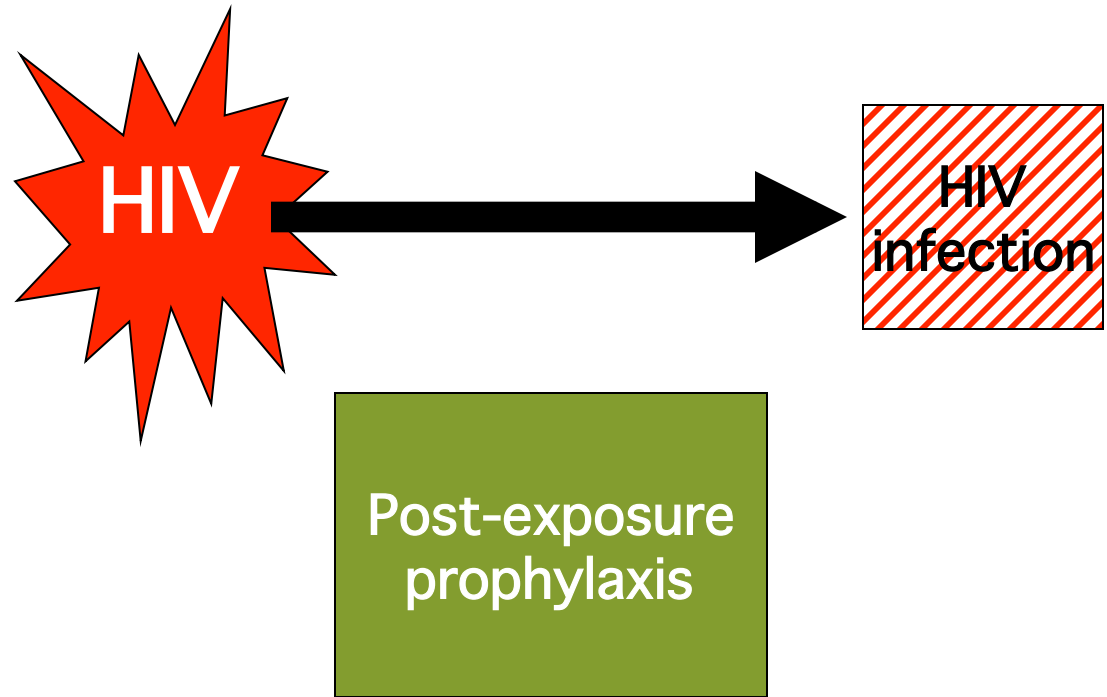
# Pre vs. Post-exposure prophylaxis



# Pre vs. Post-exposure prophylaxis



# Pre vs. Post-exposure prophylaxis



0

36

72

1

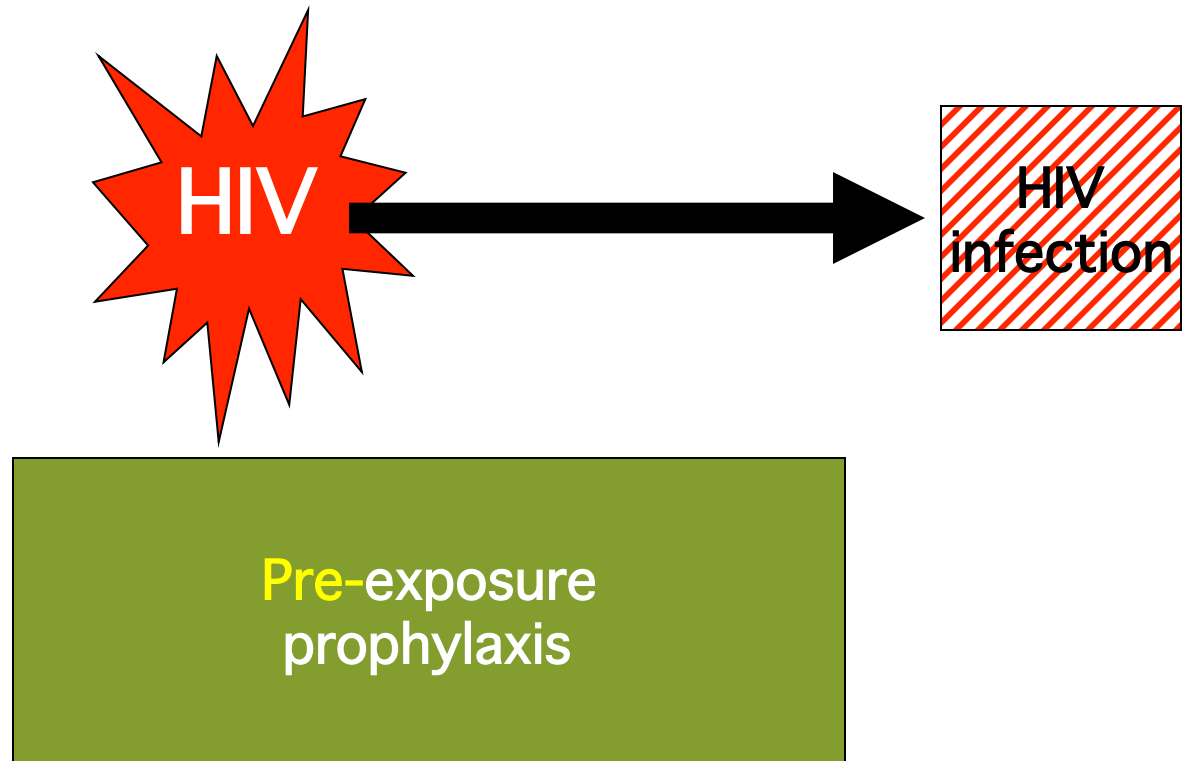
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5

HOURS

MONTHS

# Pre vs. Post-exposure prophylaxis



0

36

72

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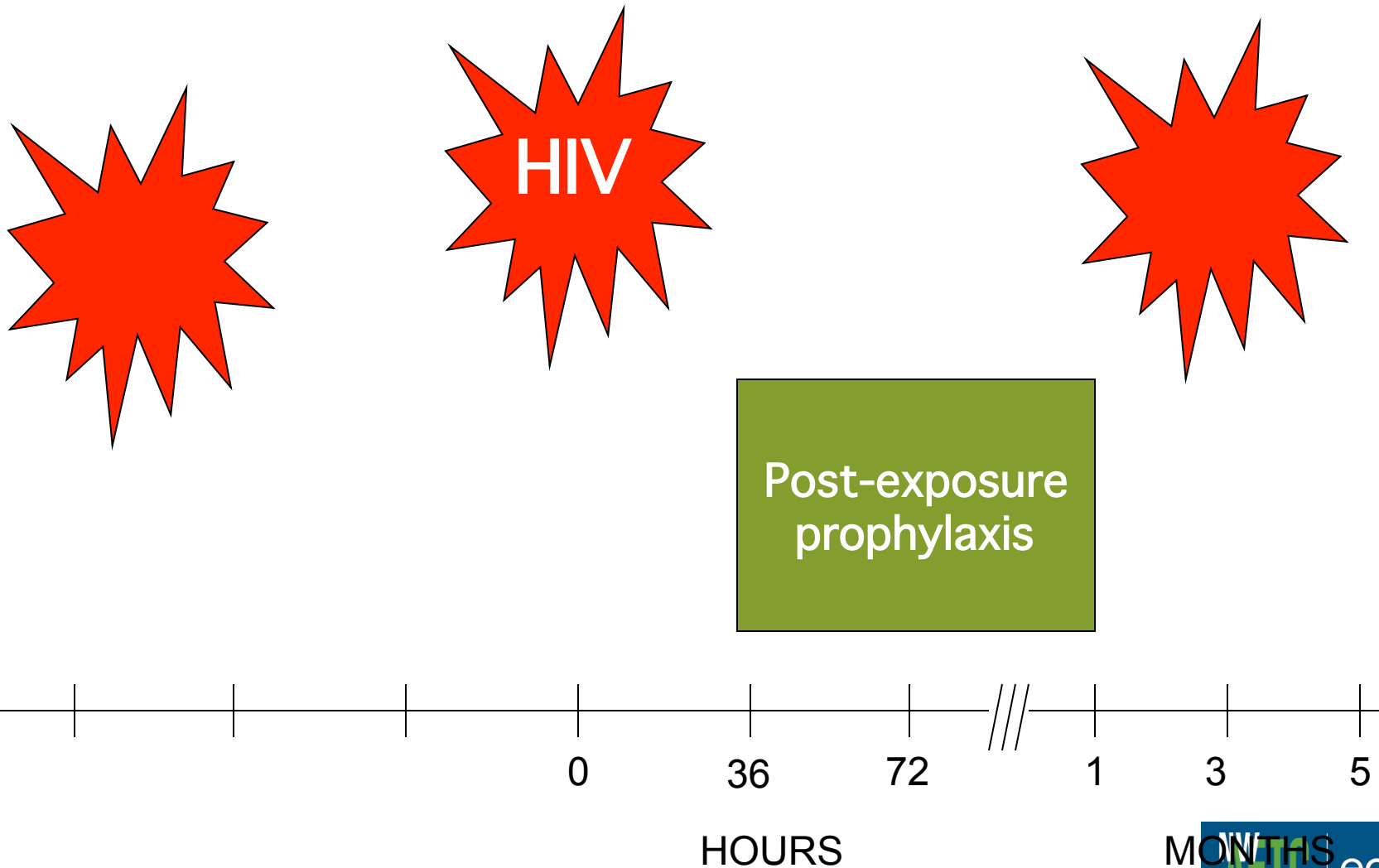
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HOURS

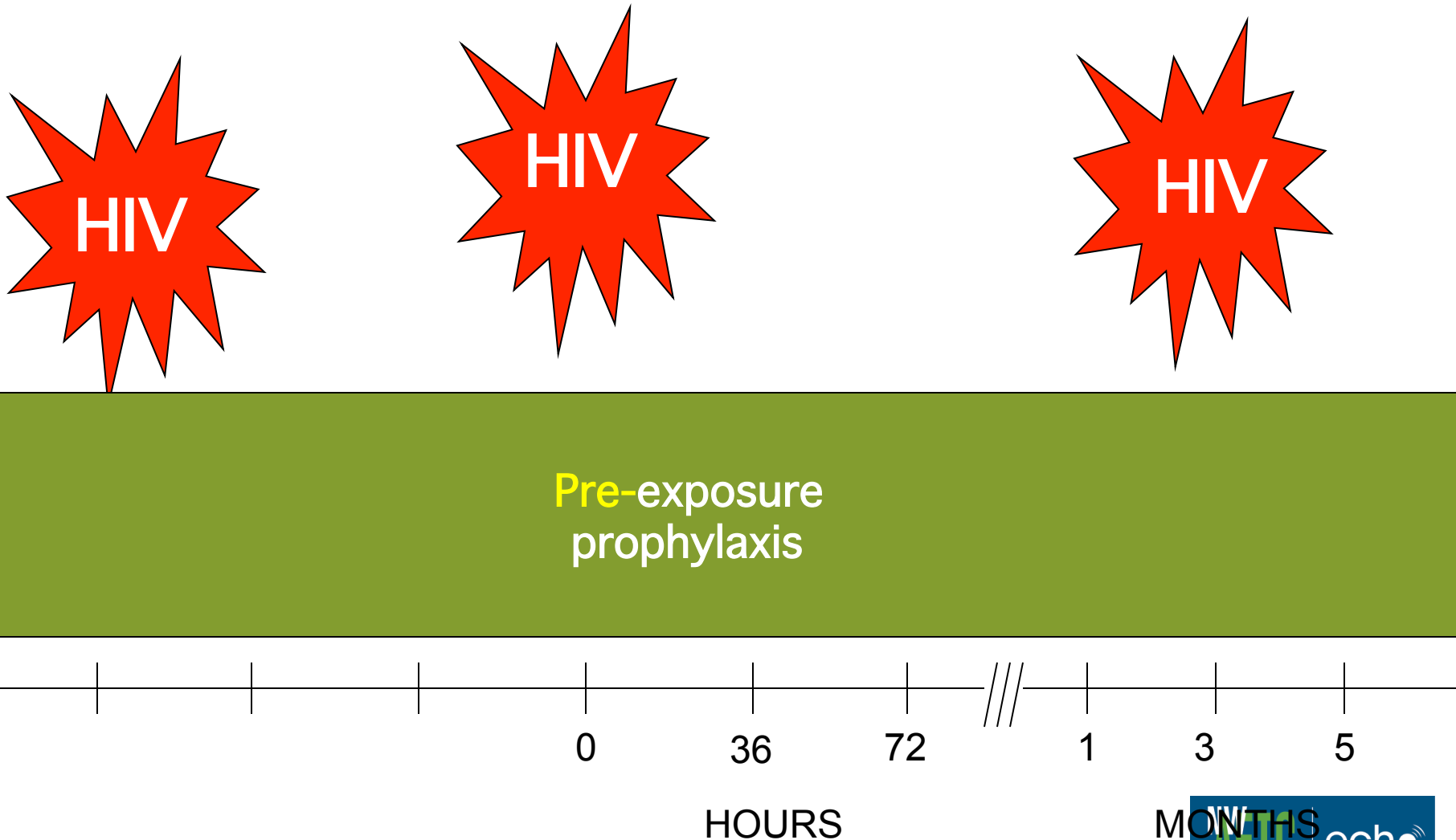
MONTHS



# Pre vs. Post-exposure prophylaxis



# Pre vs. Post-exposure prophylaxis



# PrEP medications

- Among the anti-HIV medications currently available, PrEP based on the medication tenofovir has been tested most widely:



= TDF (tenofovir)  
sold under the trade name Viread



= FTC/TDF (co-formulated emtricitabine + tenofovir)  
sold under the trade name Truvada

## ✓ **Potent:**

- Broad antiviral activity (all HIV subtypes)
- Could block initial infection (act early in HIV life cycle)
  - Relatively rapidly active

## ✓ **Safe:** Favorable safety and tolerability

✓ **Easy:** Low pill burden, no food restrictions, few drug interactions

# iPrEx study: FTC/TDF PrEP for MSM

## iPrEx: Daily oral FTC/TDF PrEP

- ✓ **2499 MSM**, randomized 1:1 daily oral FTC/TDF vs placebo
- ✓ **11 sites** (Brazil, Ecuador, Peru, South Africa, Thailand, US)
  - 9% from the US, most from Peru
- ✓ **Young high risk MSM:**
  - 50% <25 yrs
  - Median 18 partners in 12 wks prior to enrollment
  - 60% with unprotected receptive anal sex in prior 12 wks

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### Preexposure Chemoprophylaxis for HIV Prevention in Men Who Have Sex with Men

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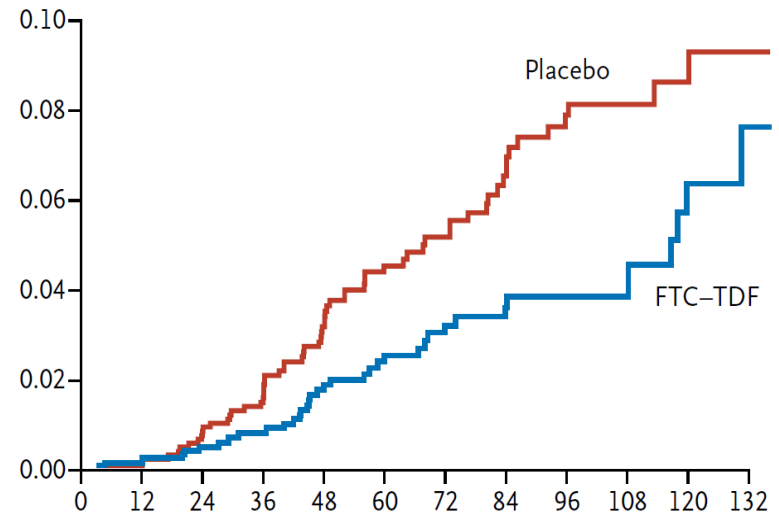
# iPrEx Efficacy

**100 infections after  
randomization**

**36 on  
FTC/TDF**

**64 on  
placebo**

**Efficacy estimate (mITT):  
44% reduction in HIV acquisition  
(95% CI 15%-63%)**



# Partners PrEP Study



PARTNERS PrEP STUDY

**4758 HIV serodiscordant couples  
(HIV+ partner not yet medically eligible for ART)**



**Randomize HIV- partners  
(normal liver, renal, hematologic function)**



**TDF once daily**



**FTC/TDF once daily**



**Placebo once daily**

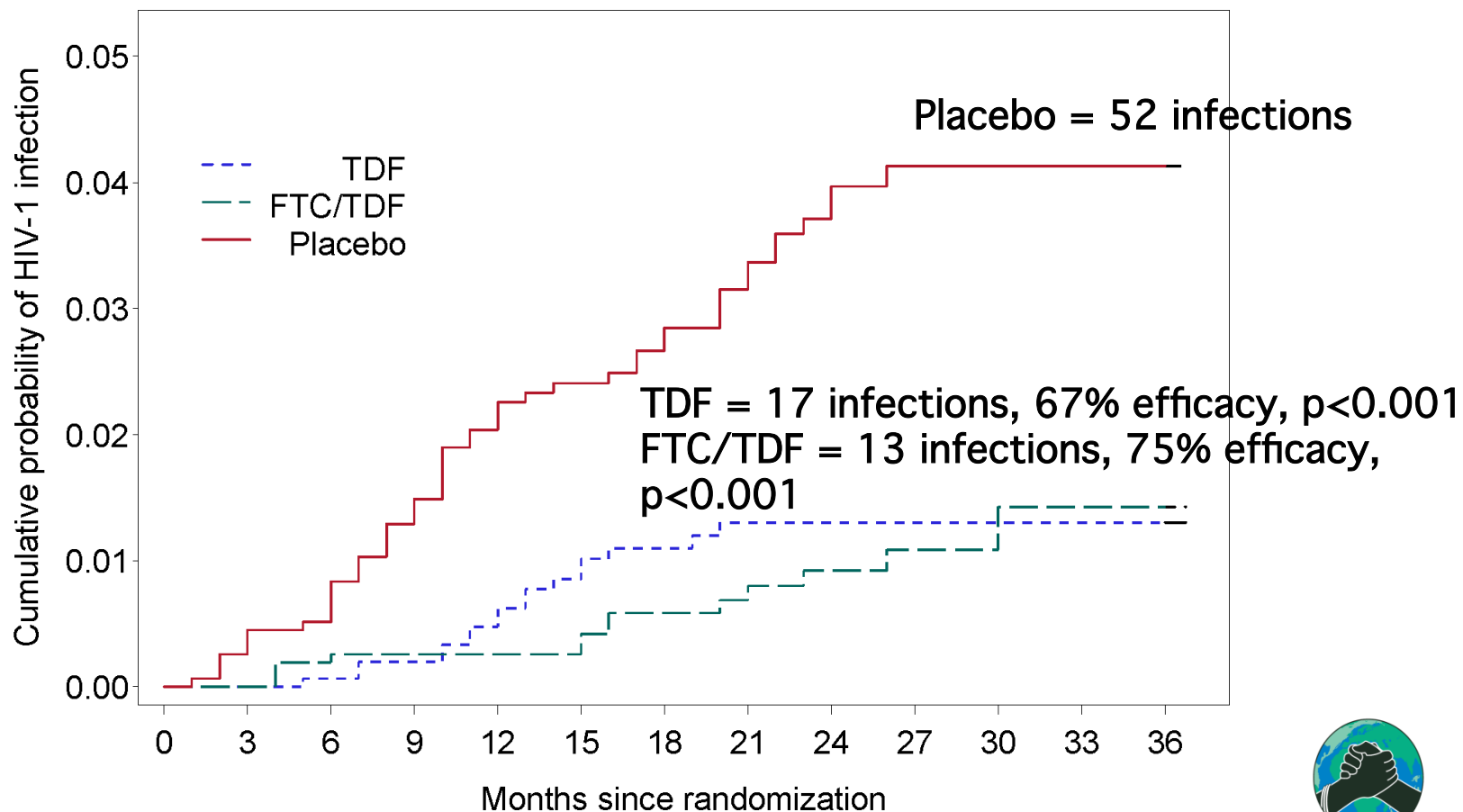
*All receiving comprehensive*



*HIV prevention services*

**Follow couples for up to 36 months**

# Partners PrEP Study: efficacy results



No. at risk:													
TDF	1572	1559	1547	1498	1350	1223	1062	902	735	510	287	108	15
FTC/TDF	1568	1557	1546	1493	1371	1248	1059	901	743	525	291	114	16
Placebo	1568	1557	1544	1487	1347	1224	1061	902	744	523	295	120	18



PARTNERS PrEP STUDY

# Tenofovir levels and HIV protection

- Objective adherence measures from trials show that when PrEP was taken (=detected in blood), protection appeared to be very high

	% with tenofovir detected	HIV-1 protection: detection versus no detection of tenofovir	
		Protection	p-value
iPrEx	51%	92%	<0.001
Partners PrEP FTC/TDF arm	81%	90%	0.002



# Key secondary questions

- SAFETY –
  - In PrEP trials, PrEP was very safe.
  - Nausea and other GI side effects in a minority (<10%), mild and primarily during first month.
  - Renal safety monitored closely in trials – no increase in renal side effects seen but TDF requires normal renal function and ongoing monitoring.
- ANTIRETROVIRAL RESISTANCE –
  - Use of PrEP medications in persons with HIV infection can result in resistance. In PrEP trials, those who became infected did not have resistance, likely because they weren't taking PrEP.
  - The only cases of resistance seen were in those who had unrecognized acute HIV at the time they started PrEP (thus, started once already infected). Ongoing testing is key in persons on PrEP.

# Summary

- In two pivotal studies, PrEP, using combination FTC/TDF (Truvada®) definitively provided protection against HIV acquisition among in MSM and heterosexual men and women at risk for HIV infection, when provided in the context of other HIV prevention services.
- Expect mild (<10%) GI side effects in the first month. Like for TDF for HIV treatment, monitor renal function.
- Antiretroviral resistance in PrEP trials was rare – greatest risk is in initiating PrEP for those with acute HIV infection.
- No evidence of greater behavioral risk-taking when on PrEP.

# FDA review of PrEP for HIV prevention

- The US FDA is currently reviewing a label indication for Truvada® for HIV prevention.
- On 10 May 2012 an Advisory Committee to the FDA recommended that the label indication be added.
- If approved (FDA decision expected in June), would be the first medication approved for prevention of HIV.

# Guidelines and guidance

*Centers for Disease Control and Prevention*

**MMWR**

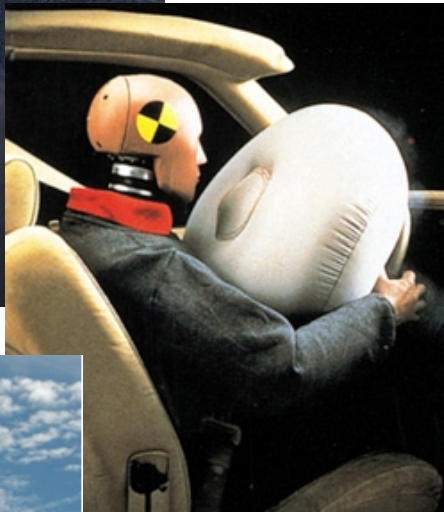
Morbidity and Mortality Weekly Report

Weekly / Vol. 60 / No. 3

January 28, 2011

## **Interim Guidance: Preexposure Prophylaxis for the Prevention of HIV Infection in Men Who Have Sex with Men**

# PrEP as part of combination HIV prevention



- There is no magic bullet for reversing the HIV epidemic
- PrEP may become part of the many things we do to try to reverse the HIV epidemic

# Questions

- Who is an appropriate patient to consider for pre-exposure prophylaxis (PrEP) for HIV prevention?
  - High risk of HIV. In the US, particular focus would be MSM, although other populations (HIV- heterosexual with HIV+ partner) important too.
- What testing is necessary before starting PrEP?  
Once on PrEP?
  - HIV testing essential. Renal function.
- What counseling messages should accompany PrEP prescribing?
  - HIV risk reduction, adherence (PrEP only works if taken).